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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,142	02/18/2004	Stephanos Kyrkanides	21108.0040U1	3987

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,142	KYRKANIDES, STEPHANOS	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-143* is/are pending in the application.

4a) Of the above claim(s) *44-71,76-82 and 92-132* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-43,72,75,83-91 and 133-143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 27, 2006 has been entered.

Claims 44-71, 76-82, 92-132 are withdrawn. Claims 1, 12, 16, 72 are amended. Claims 142, 143 are new.

It is noted that withdrawn claims 46 and 55 are amended. However, the status identifier does not indicate that the claims are amended. As such, the amendment does not comply with 37 CFR 1.121(c). Applicant must properly indicate status of the claims or risk non-entry of the amendments. See MPEP 714.

Claims 1-43, 72-75, 83-91,133-143 are under consideration.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-43, 72-75, 83-91,133-143 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

1) a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3, and wherein the second cistron encodes HEX-alpha, wherein the sequence is set forth in SEQ ID NO. 1.

2) a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-alpha, wherein the sequence is set forth in SEQ ID NO. 1, and wherein the second cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3.

3) a composition comprising a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3, and wherein the second cistron encodes HEX-alpha, wherein the sequence is set forth in SEQ ID NO. 1.

4) a composition comprising a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-alpha, wherein the sequence is set

forth in SEQ ID NO. 1, and wherein the second cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3.

does not reasonably provide enablement for

any nucleic acid construct or composition comprising a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes any HEX-alpha, other than SEQ ID NO. 1, and wherein the second cistron encodes any HEX-beta, other than SEQ ID NO. 3.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons of record, June 6, 2005 and January 27, 2006.

A new issue of enablement is as follows. Claim 1 is drawn to a composition comprising an isolated nucleic acid sequence wherein the nucleic acid comprises a sequence encoding HEX-alpha and a sequence encoding a HEX-beta. However, there is no promoter driving the expression HEX-alpha or HEX-beta. A skilled artisan would not have predicted expression of the HEX proteins in the absence of expression elements such as a promoter.

Response to Arguments

Applicant's arguments filed July 27, 2006 have been fully considered but they are not persuasive.

Applicant indicates that claims 1 and 72 have been amended to recite the functional limitation, "wherein the HEX-alpha and HEX-beta can catabolize GM_2 ganglioside." Applicant indicates that one would be able to combine the disclosed structural (i.e. sequence) and the corresponding functional (GM_2 catabolysis) characteristics of HEXA and HEXB to ascertain whether a given HEX mutant can be used in the present invention (Applicant's response, page 16, under "A. Structure and Function"). In response, screening for mutants that fit the functional criteria, as described in claims 1 and 72, do not enable an artisan to arrive at the claimed invention. Screening for sequences that are mutants of SEQ ID NO. 1 and 3 and have a particular functional activity do not enable an artisan to arrive at the claimed invention. For further discussion, see Written Description, below.

With regard to the issue of enablement of HEX proteins which are 70-95% identical to SEQ ID NO. 1 or to SEQ ID NO. 3, Applicant indicates that as demonstrated in the article provided in the Applicant's response on November 9, most (about 90%) mutants will maintain enzyme function with sequence identities as low as 60% and in fact enzyme function does not generally start to diverge until the sequence identity is below 70% (Tian, et al., 2003, J. Mol. Biol., 333: 863-882, provided by Applicant) (Applicant's response, Applicant's emphasis, page 16, under "B. Percent Homology"). While Applicant provides this argument, it is not persuasive. While Tian et al. generally indicates that enzyme function starts to diverge quickly when the sequence identity is

below 70% (Tian et al., abstract), nothing in the specification or the art what of that 70% of HEXA and HEXB would need to be conserved such that an artisan would arrive at mutants of HEXA and HEXB with activity. Even while Tian et al. indicates that enzyme function diverges when the sequence identity is below 70%, it is noted that Tian et al. teach that most homologous proteins have different functions, which makes the inference of functional similarity from sequence similarity difficult and problematic (Tian et al., page 863, 2nd col., 1st parag.). Tian et al. also indicate that the relationship between functional divergence and sequence divergence is not in fact clear and that using only sequence similarity to classify protein families might result in one family being liked to different kinds of function (Tian et al., page 864, 2nd col., 3rd parag.). Subsequently, Tian et al.'s teaching indicates that it is not readily apparent how an artisan would arrive at the scope of mutant HEXA and HEXB that catabolize GM_2 ganglioside. With regard to Applicant asserting that while "most" protein mutants may maintain enzyme function, the assertion does not indicate to an artisan how to discriminate the 10% of mutants which do not have activity. While one might assert that an artisan could screen for mutants, screening without guidance as to what structure of HEXA and HEXB would need to be conserved to arrive at a functional protein is not enabled. For further discussion on the issue of screening, see the Written Description rejection, below. As such, the specification and art do not enable an artisan to arrive at the claimed invention.

Thus, the claims remain rejected.

Claims 1-43 72-75, 83-91, and 133-141 remain rejected in modified form under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record, June 9, 2005 and January 27, 2006.

Response to Arguments

Applicant's arguments filed July 27, 2006 have been fully considered but they are not persuasive.

Applicant indicates that claims 1 and 72 have been amended to recite the functional limitation, "wherein the HEX-alpha and HEX-beta can catabolize GM_2 ganglioside." Applicant indicates that one would be able to combine the disclosed structural (i.e. sequence) and the corresponding functional (GM_2 catabolysis) characteristics of HEXA and HEXB to ascertain whether a given HEX mutant can be used in the present invention (Applicant's response, page 16, under "A. Structure and Function", also page 17, under "IV. Rejection under 35 U.S.C. § 112, first paragraph-Written Description"). In response, while it is understood that the amendment is written to limit the claimed invention to HEX-alpha and HEX-beta with a particular functional activity, nothing in the specification or the art indicate what region(s) of HEX-alpha or HEX-beta is the domain(s) that provides the activity of catabolizing GM_2, such that an artisan could reasonably predict that targeting certain residues would affect enzymatic

activity. While Applicant indicates that an artisan could ascertain whether a certain HEX mutant can be used in the present, screening for these mutants based on enzymatic activity is not adequate written description.

According to MPEP 2163,

> An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.").

As such, the claims, as they apply to this issue, remain rejected.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

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PRIMARY EXAMINER